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DEPARTMENT OF HEALTH
DRUG OFFICE
DRUG REGISTRATION AND IMPORT/EXPORT CONTROL DIVISION
3/F., Public Health Laboratory Centre,
382 Nam Cheong Street, Kowloon, Hong Kong

BY FAX

11 January 2016

Dr. Donald LI
President
Hong Kong Academy of Medicine
(Fax Number: 2505 5577)

Dear Dr. LI,

Deferasirox: Risk of pancreatitis in paediatric patients

Your attention is drawn to Singapore Health Sciences Authority's (HSA) announcement regarding the risk of pancreatitis associated with the use of deferasirox in paediatric patients.

Deferasirox (Exjade®, Novartis (Singapore) Pte Ltd) is an orally active iron chelator that has been registered in Singapore since 2008. It is approved for the treatment of chronic iron overload.

Acute pancreatitis is usually characterised by abdominal pain and an increase in pancreatic enzymes in the blood and urine, with an overall mortality of approximately 5%. Epidemiological studies suggest that drug-induced pancreatitis is relatively rare, with an estimated incidence of 0.1% to 2%. Although most cases of possible drug-induced pancreatitis are mild, some have been reported to be severe or even fatal. The management of drug-induced pancreatitis includes the discontinuation of suspected drugs to prevent further progression of any ongoing pancreatic injury, intravenous fluid replacement, and close monitoring of blood pressure, cardiac and pulmonary status. In more severe cases, parenteral or enteral nutrition may be required if patients are unable to tolerate oral intake.

Recently, overseas adverse reaction reports received through the World Health Organisation (WHO) VigiBase® suggest a signal of pancreatitis associated with the use of deferasirox in paediatric patients.

As of March 2015, 14 reports of pancreatitis associated with the use of deferasirox in children and adolescents, aged between 4 to 16 years old, have been identified from VigiBase®. Deferasirox was the only suspected drug in 11 of these 14 cases. The remaining three cases also included other suspected drugs, such as azithromycin, ceftriaxone, hydroxycarbamide, amoxicillin, clarithromycin, omeprazole and deferoxamine. The time to onset was reported in nine cases and ranged from 17 days to over five years (median 11 months). This time interval is relatively consistent with the time to onset of drug-induced pancreatitis that had been reported in literature with various drugs including valproic acid, oestrogen, sulindac, statins and ACE inhibitors. In addition, a positive dechallenge was also noted in six cases, which is supportive of a drug-induced effect.

HSA has not received any reports of pancreatitis associated with the use of deferasirox in Singapore. The package insert for Exjade® is currently in the process of being strengthened to include warnings on the risk of acute pancreatitis.

Healthcare professionals are advised to take into consideration the potential risk of acute pancreatitis in patients who are prescribed deferasirox, and to monitor for signs and symptoms which could be suggestive of pancreatitis, such as abdominal pain, nausea, vomiting or tenderness of the abdomen to touch, particularly in paediatric patients.

Please refer to the HSA's website for details:

http://www.hsa.gov.sg/content/hsa/en/Health_Products_Regulation/Safety_Information_and_Product_Recalls/Product_Safety_Alerts/2015/risk-of-pancreatitisassociatedwiththeuseofdeferasiroxinpaediatri.html

In Hong Kong, there are three registered pharmaceutical products containing deferasirox, namely Exjade Dispersible Tab 125mg (HK-54548), 250mg (HK-54547) and 500mg (HK-54549). All products are prescription only medicines registered by Novartis Pharmaceuticals (HK) Limited. The products are indicated in the management of chronic iron overload, either in patients with transfusion-dependent anaemias aged 6 years or older, or in patinets with transfusion-dependent anaemias aged two to five who cannot be adequately treated with deferoxamine. The products are also indicated for the treatment of chronic iron overload in patients with non-transfusion-dependent thalassemia syndromes aged 10 years and older. So far, the Department of Health (DH) has received one adverse drug reaction case related to deferasirox, but it was not related to acute pancreatitis. In view of the HSA announcement, the matter will be discussed by the Registration Committee of the Pharmacy and Poisons Board. Healthcare professionals are advised to balance the risk of possible adverse effects against the benefit of treatment.

Please report any adverse events caused by drugs to the Pharmacovigilance Unit of the DH (tel. no.: 2319 2920, fax: 2319 6319 or email: adr@dh.gov.hk). For details, please refer to the website at Drug Office under "ADR Reporting": http://www.drugoffice.gov.hk/adr.html. You may wish to visit the Drug Office's website for subscription and browsing of "Drug News" which is a monthly digest of drug safety news and information issued by Drug Office.

Yours sincerely,

(Grant NG)
for Assistant Director (Drug)